



**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460**

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

10/13/11

MEMORANDUM

SUBJECT: **Silver Zeolite X.** Evaluation of Sinanen's response to the Agency memorandum concerning waiver requests, test substance identification, and data bridging for toxicology studies supporting registration applications for Zeomic Type HJ and HW Silver Zeolite X Products.

| | |
|------------------------------------|---|
| PC Code for Silver: 072501 | DP Barcode No.: D395093 |
| PC Code for [Silver] Zeolite X: NA | EPA Registration Nos.: 87731-R and 87731-E |
| Decision Nos.: 433514 | Regulatory Action: New product registration (Section 3) |
| Petition No(s): NA | Case No.: NA |
| Risk Assess Type: NA | CAS No.: 1318-02-1 (includes Zeolite X) |
| | 7440-22-4 (Silver) |
| | 68989-22-0 (Zeolite X as a pure inert) |
| TXR No.: 1,003,222 | 40 CFR: NA |
| MRID No.: NA | |

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INTRODUCTION

This memorandum concerns FIFRA section 3 registration of Zeomic Type HJ Silver Zeolite X and Zeomic Type HW Silver Zeolite X (EPA Reg. Nos. 87731-R and 87731-E, respectively) (formerly 71227-O and 71227-I, respectively). These pending products are proposed to serve as preservatives incorporated into nonfood-contact polymeric products. Additional information has been submitted by Technology Sciences Group, Inc. (TSG) representing Sinanen Zeomic Co., Ltd. (formerly Sinanen Company, Ltd.). TSG's 8/1/11 letter to M. Swindell of EPA was in response to a FAX of a 7/11/11 draft EPA evaluation of these two registration applications. The draft EPA memorandum was finalized 8/8/11 with

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no substantive changes (W. Hazel, D378847 and D378912). The EPA memorandum identified several pieces of information needed to permit the Agency to determine whether there is substantial similarity between Metal-Zeolites A and X which would, in turn, permit decisions to be made regarding Sinanen's waiver requests and toxicology data bridging request.

SUMMARY OF SUBMITTED INFORMATION

To permit the Agency to determine whether there is substantial similarity between Metal-Zeolites A and X, Sinanen Co. has submitted information to address the deficiencies cited in the 8/8/11 EPA memorandum. This consisted of several structural and physical properties and a comparison of the acute toxicity studies conducted on three of Sinanen's registered Zeolite A products and their two pending Zeolite X products. The properties are presented in Table 1 (excerpted from the 8/8/11 EPA review) with Sinanen's new information in shaded cells. The acute toxicity comparison in Table 2 is taken from TSG's 8/1/11 letter.

Table 1. Comparison of Zeolite A and X structural and physical properties.

| Property | Zeolite A | Zeolite X (published) | Zeolite X (Sinanen) ^b |
|--|---|--|---|
| Formula of periodic building unit | Na ₁₂ [(AlO ₂) ₁₂ (SiO ₂) ₁₂]•27 H ₂ O | Na ₈₆ [(AlO ₂) ₈₆ (SiO ₂) ₁₀₆]•264H ₂ O | Na ₁₂ (AlO ₂) ₁₂ (SiO ₂) ₁₂ •27H ₂ O or Na ₂ O•Al ₂ O ₃ •2.4SiO ₂ |
| Pore opening of the Na ⁺ form | 4.2 Å | 8 Å | 7.2 Å |
| IZA Framework Type Code | LTA | FAU | FAU |
| Crystal system | Cubic | Cubic | Cubic |
| No. β-cages/cube face ^a | Four | Six | Six |
| Channel sides | 8-ring | 12-ring | 12-ring |
| Cation Exchange Capacity (CEC) | 5.48 meq/g | 4.73 meq/g | 4.7 meq/g |
| Cavity diameter | 11.4 Å | 13 Å | 13 Å |

^aA β-cage is a 14-faced 3-dimensional structure having eight 6-sided faces and six 4-sided faces. Its chemical composition as a mineral in the sodium form is Na₆[Al₆Si₆O₂₄].

^bInformation in shaded cells is from the 8/1/11 TSG letter on behalf of Sinanen Zeomic Co., Ltd.

Table 2. Comparison of acute toxicity studies for Sinanen's Zeolite A and X products.^a

| EPA reg. no. | Sinanen Company – Zeolite A Products | | | Sinanen Zeomic Co. – Zeolite X | |
|------------------|--------------------------------------|-------------------------|-------------------------|--------------------------------|-------------------------|
| | Type AK | Type AJ | Type AC | Type HJ | Type HW |
| | 72854-4 | 72854-1 | 72854-7 | 87731-R | 87731-E |
| Silver | 4.93% | 2.5% | 3.52% | 0.5% | 2.2% |
| Zinc | 12.90% | 14.4% | -- | 7.0% | 7.0% |
| Copper | -- | -- | 6.1% | -- | -- |
| LD ₅₀ | >2000 mg/kg | >5000 mg/kg | >5000 mg/kg | >2000 mg/kg | >2000 mg/kg |
| Acute Oral Rat | bw in males and females | bw in males and females | bw in males and females | bw in males and females | bw in males and females |
| MRID | 452521-02 | 44644-01 | 416158-02 | 484358-01 | 484358-01 |

| EPA reg. no. | Sinanen Company – Zeolite A Products | | | Sinanen Zeomic Co. – Zeolite X | |
|---|--------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| | Type AK | Type AJ | Type AC | Type HJ | Type HW |
| | 72854-4 | 72854-1 | 72854-7 | 87731-R | 87731-E |
| Silver | 4.93% | 2.5% | 3.52% | 0.5% | 2.2% |
| Zinc | 12.90% | 14.4% | -- | 7.0% | 7.0% |
| Copper | -- | -- | 6.1% | -- | -- |
| LD ₅₀ Acute Dermal Rat | >2000 mg/kg bw in males and females | >2000 mg/kg bw in males and females | >5000 mg/kg bw in males and females | >2000 mg/kg bw in males and females | >2000 mg/kg bw in males and females |
| MRID | 452521-03 | 446644-01 | 416158-03 | 484358-05 | 484358-05 |
| LC ₅₀ Acute Rat Inhalation | >2.86 mg/L | -- | >2.59 mg/L | >2.31 mg/L in males and females | >2.31 mg/L in males and females |
| MRID | 450243-02 | 416158-04 | 416158-04 | 484358-02 | 484358-02 |
| Rabbit Eye Irritation | Category I ocular irritant | -- | Moderate irritant | Mildly irritating | Mildly irritating |
| MRID | 450243-05 | 416385-01 | 416385-01 | 484358-03 | 484358-03 |
| Rabbit Dermal Irritation | Primary irritation index = 3.03 | Primary irritation index = 0 | Primary irritation index = 0.08 | Primary irritation index = 0 | Primary irritation index = 0 |
| MRID | 450243-06 | 446644-02 | 416158-05 | 484358-04 | 484358-04 |
| Dermal Guinea Pig Sensitization | Not a sensitizer | Not a sensitizer | Not a sensitizer | Not a sensitizer | Not a sensitizer |
| MRID | 450243-03 | 416158-06 | 416158-06 | 484358-06 | 484358-06 |

^aAcute toxicity summary from 8/1/11 TSG letter on behalf of Sinanen Zeomic Co., Ltd.

CONCLUSIONS

a. Physical/chemical properties.

As per the shaded cells of Table 1, information on the following has been submitted by TSG on behalf of Sinanen to support registration of their Zeolite X products: pore opening of the Na⁺ form, IZA Framework Type Code, crystal system (revised from spherical to cubic), number of β-cages/cube face (revised from four to six), channel sides, cation exchange capacity, and cavity diameter. These are among the types of information needed to allow EPA to make decisions regarding test substance identification, toxicology data waiver requests and toxicology data bridging.

The structural and physical information provided agree quite closely with the published characteristics of Zeolite X. However, the differences between Zeolites X and A noted in the 8/8/11 EPA memorandum remain. Upon reassessment, the main difference between Zeolites A and X remains the pore diameters which are 4.2 Å and 7.2 Å, respectively. Neither pore diameter is expected to significantly impede the exchange of the silver ion (Ag⁺) which has an ionic radius of 1.28 Å. As in the original Sinanen registration application, the 8/1/11 TSG letter mentions the similar leaching rates of silver and zinc ions from Zeolites A and X. It appears

to be the type of linkage between adjacent β -cages (double four-membered rings in Zeolite A and double six-membered rings in Zeolite X) that causes the difference in pore diameter as well as all other structural differences between Zeolites A and X. Otherwise there appears to be no substantive differences between Zeolites A and X. The CEC's of both are quite a bit higher than those of most soils but they are similar to each other. Although there are structural differences between Zeolites A and X, the influence of these properties on toxicity cannot be directly determined without testing.

b. Toxicology.

As is evident from Table 2, both pending Zeolite X products have either no toxicity at a limit dose of 2,000 mg/kg or acute toxicities are very similar to, or less than, those of Zeolite A products.

It was specified in a 12/7/10 letter from Mark Hartman of AD to Gary Burin of TSG that a 90-day inhalation toxicity study conducted using Silver Zeolite A as test substance would be the only additional mammalian toxicity study required to support registration of all antimicrobial active ingredients consisting of Zeolite A containing one or more of the following metal ions: Ag, Cu, or Zn. Sinanen has requested to bridge already submitted and accepted toxicology data conducted using Metal-Zeolite A materials as test substance to support registration of their pending Silver Zeolite X products. In addition, Sinanen requests a waiver from the requirement to conduct a subchronic dermal toxicity study, the acute + subchronic neurotoxicity studies, and the immunotoxicity study.

The Agency has determined that there is substantial similarity between Zeolites A and X from a generic mammalian toxicity perspective. Sinanen's request to bridge already submitted and accepted toxicology data conducted using Metal-Zeolite A materials as test substance to support registration of their pending Silver Zeolite X products is granted. Sinanen's request for a waiver from the requirement to conduct a subchronic dermal toxicity study, the acute + subchronic neurotoxicity studies, and the immunotoxicity study are granted. The Agency agrees that the 90-day inhalation toxicity study [to be] conducted using Silver Zeolite A as test substance may be bridged to Silver Zeolite X. However, EPA reserves the right, as always, to require any studies deemed necessary in the future using Sinanen's Silver Zeolite X as test substance.

Sign-off Date : 10/13/11
DP Barcode No. : D395093

TXR No. : 1,003,222



13544

R195249

Chemical Name: Silver

PC Code: 072501

HED File Code: 90125 AD RASSB Tox Correspondence

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